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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BURKHART, MICHAEL D	
ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
12/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/072,036	THASTRUP ET AL.	
	Examiner	Art Unit	
	Michael D. Burkhart	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-72* is/are pending in the application.

4a) Of the above claim(s) *55-72* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

In view of the Pre-Appeal Brief Conference decision dated 10/12/2007, the finality of the previous Office Action is withdrawn and prosecution is hereby reopened. New grounds of rejection are set forth below.

Claims 44-72 are pending. Claims 55-72 remain withdrawn as drawn to a non-elected invention. Claims 44-54 are under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 48 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This rejection is maintained for reasons made of record in the Office Action dated 5/30/2007, which are reiterated below.**

Amended claim 48 recites a "synthetic chemical compound". The response does not indicate specifically where in the specification support may be found for the limitation, which is intended to be a narrowing limitation of the compounds recited in the base claims 44-46 (see page 12 of the response dated 3/20/2007). A review of the specification does not reveal any

support for "synthetic chemical compounds" as a narrowing limitation of the library of compounds recited in the base claims. In fact, a search of the specification does not reveal use of the word "synthetic." Therefore, there is no support for the limitation "synthetic chemical compound." Thus, the amended claim includes impermissible New Matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 44-52 are rejected under 35 U.S.C. 102(b) as being anticipated by Htun et al (PNAS, 1996, cited by applicants, IDS of 2/5/2002) as evidenced by Carey et al (1996, of record) or Agarwal (Pharmacol. Ther., 1996). **This is a new rejection.**

Htun et al disclose a fusion protein of glucocorticoid receptor and GFP (GR-GFP) that was transfected into murine 1471.1 cells that were treated with dexamethasone, RU486, progesterone, or 17b-estradiol in order to determine the effects of these compounds on the translocation of the GR-GFP fusion protein from the cytoplasm into the nucleus (see the abstract, Figs. 1-3 and 5, and page 4847, second column, third full ¶). The measurement of translocation was done by determining a "variation" of GR-GFP location (either cytoplasmic or nucleic) using time-lapse video microscopy and quantitated by recording microscopic images followed by analysis of the images with custom software from G.W. Hannaway & Associates (see section entitled "Image Acquisition and Analysis", first column, page 4846). The collection of steroid

hormones (e.g. dexamethasone, progesterone,etc.) tested by Htun et al is considered to be a "library of compounds", and the methods of Htun et al cited above are considered "screening a library of compounds" according to the arguments set forth in the Ireland Declaration dated 3/20/2007.

Carey et al teach that GR-GFP (or wild type GR) inherently binds the Ran/TC4 GTPase (Ran). Dominant negative mutants of the enzyme Ran were used to identify wild-type Ran as responsible for nuclear import of the GR-GFP protein (see abstract, paragraph bridging first and second columns page 986, and last paragraph, first column, page 994 of Carey et al). Thus, Ran/GR-GFP is a component of the glucocorticoid receptor signaling pathway, with Ran and GR-GFP being subunits of the component. Furthermore, Agarwal teaches that GR inherently binds heat shock proteins in the cytoplasm (¶ linking first and second columns, page 186 and Fig. 1). Thus, heat shock protein(s)/GR is a component of the glucocorticoid receptor signaling pathway, with heat shock protein(s) and GR being subunits of the component.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 44-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Htun et al (PNAS, 1996, cited by applicants, IDS of 2/5/2002) as evidenced by Carey et al (1996, of record) in view of Agarwal (Pharmacol. Ther., 1996) and Sonenberg et al (U.S. Patent 5,874,231, effective filing date 8/22/1994). **This is a new rejection.**

The teachings of Htun et al, Carey et al , and Agarwal et al are set forth above and applied as before. In one interpretation, the set of steroid hormones used by Htun et al would not constitute a "library of compounds" due to the number of compounds used by Htun et al, i.e. four distinct steroid hormones. Thus, one of skill in the art might consider a "library of compounds" to necessarily comprise more than four distinct compounds, although the instant specification and the Ireland Declaration are silent as to how many compounds must be included in order to teach a "library of compounds." Htun et al further teach that their methods of using the GR-GFP fusion protein to study GR receptor translocation and function are a powerful and useful approach to solving several problems in hormone receptor biology (page 4845, first and second columns), and yield distinct nuclear localization results for different receptor ligands (e.g. Fig. 5, dexamethasone vs. RU486). In summary, Htun et al indicate their method is an invaluable tool for further studies of many aspects of hormone receptor biology (page 4850, first column, fourth full ¶).

Agarwal teaches that many glucocorticoid antagonists (i.e. GR receptor antagonists) were well known at the time of the instant invention, and of the desirability of antiglucocorticoids, such as RU486, for use in the therapy of a number of diseases. See in particular Figure 2; page 188, second column; and page 199, second column, third full ¶ to page 200.

Sonenberg et al teach methods for screening compound libraries for ligands of steroid receptors in order to identify agents (or lead agents) potentially useful in the treatment of hormone disorders. See in particular the abstract and column 24, line 35 to column 25, line 27.

The claimed methods are essentially disclosed by Htun et al, with the exception that a "library of compounds" may be interpreted to be larger in number than the four steroid hormones used by Htun et al. The ordinary skilled artisan, seeking methods to study the biology of the GR receptor, or to identify agents with antiglucocorticoid activity, would have been motivated to use the compound libraries taught by Sonenberg et al with the methods of Htun et al because Htun et al teaches their method to be useful and efficient in characterizing the translocation and activity of the GR receptor in response to agonists and antagonists. It would have been obvious for the skilled artisan to do this because of the known benefit of studying the GR receptor response to such agents, as taught by Htun et al; or, alternatively, in order to identify useful antiglucocorticoid agents, as taught by Agarwal et al. Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 53 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Htun et al, Carey et al, Agarwal, and Sonenberg et al as applied to claims 44-52 above, and further in view of Cormack et al (Gene, 1996, of record). **This is a new rejection.**

The teachings of Htun et al, Carey et al, Agarwal, and Sonenberg et al are described above and applied as before. None of these references teach the use of GFP with an F64L mutation.

Cormack et al teach mutations of GFP, including the F64L and S65T (Table 1) substitutions in GFPmut1, which had a 35-fold increase in fluorescence intensity relative to wt GFP (Table II, page 37). Cormack et al teach these GFP mutants to have wide applicability in any GFP study (page 38, first column, number (4)), that they fluoresce more intensely, and are more stable due to efficient folding (abstract and paragraph linking pages 33 and 34).

The claimed methods are essentially disclosed by Htun et al, Carey et al, Agarwal, and Sonenberg et al with the exception of the GFP F64L substitution. The ordinary skilled artisan, seeking a method to detect translocation of GFP-tagged proteins would have been motivated to use GFP F64L/S65T substitution (or the other GFP mutants) with the detection methods of Htun et al because Cormack et al teaches them to be well known types of GFP proteins that have utility for detection in cell culture and to have superior fluorescence and stability properties. It would have been obvious for the skilled artisan to do this because of the known benefit of using a GFP protein with superior fluorescence and stability as taught by Cormack et al. Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the ordinary

skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhart whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michael D. Burkhart
Examiner
Art Unit 1633

/Joseph Woitach/
Joseph Woitach
SPE 1633